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May 24, 2018

Warren Casey, PhD
Director, NICEATM
National Institute of Environmental Health Sciences
P.O. Box 12233
Durham, NC USA 27709

RE: ICCVAM; Notice of Public Meeting; Request for Public Input

Dear Dr. Casey,

On behalf of the Humane Society of the United States (HSUS) and our members and supporters, we appreciate the opportunity to provide comments on Interagency Coordinating Committee on the Validation of Alternative Methods' (ICCVAM's) recent activities as well as its future direction. HSUS commends ICCVAM on its publication of *A Strategic Roadmap for Establishing New Approaches to Evaluate the Safety of Chemicals and Medical Products in the United States*, which is a major step toward implementing the vision of a more human-relevant, predictive, and economical approach to chemical safety evaluation while reducing animal use. The "Roadmap" clearly lays out an organized and transparent set of goals and identifies the broad steps that will be needed to achieve these goals.

Strategic goal: Connect end-users with the development of new tools

A key strategy in the Roadmap is connecting new approach methodology (NAM) developers with end users, for example, industry and regulatory agencies, as well as engaging the participation of all stakeholders. We have already seen examples of this in the recent efforts of ICCVAM and the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) to reduce animal use in acute toxicity testing, including:

- NICEATM's leadership in convening a workshop of global regulators to consider NAMs for skin sensitization, which resulted in a comprehensive review of international data requirements, a review of the existing animal test data, and has spurred approval of Organisation for Economic Cooperation and Development (OECD) guidelines and guidance documents as well as acceptance of these methods by the OECD and some member countries.
- The workshop held in April 2018 on Predictive Models for Acute Oral Systemic Toxicity, which was a successful forum that facilitated

exchange of knowledge and information needs among federal agencies, industry, academia, and other stakeholders. We believe this kind of early exchange is critical for faster adoption and hope this will be a model for future endeavors to develop and implement NAMs in a regulatory context.

Identify anticipated testing requirements.

Another key strategy outlined in the Roadmap is to identify anticipated agency testing requirements and delineate testing requirements and context of use. In its efforts to review agencies' data requirements, we urge ICCVAM to invite the agencies to consider information needs rather than simply review historical test usage, which will enable the development of NAMs that better address agency mandates to protect human and environmental health.

That said, recent efforts to retrospectively review test method performance, including whether results have actually been integral to hazard or risk assessment, have been impactful in replacing these tests. Two examples are the decision by EPA's Office of Pesticide Programs (OPP) to waive the acute dermal test for pesticide formulations¹ and the interim policy issued by both OPP and the Office of Pollution Prevention and Toxics (OPPT) to accept two NAMs for skin sensitization assessment. Retrospective reviews of historically used animal tests can not only identify tests that contribute little to hazard or risk assessment, but can also provide valuable information regarding comparator performance when evaluating NAMs. ICCVAM should continue to support and conduct these reviews.

In reviewing agency's information needs, we hope that ICCVAM will also consider impact on animal use when prioritizing areas of focus. For example, ICCVAM previously identified vaccine preparation and evaluation as a priority for NAM development due to the large numbers of animals and animal welfare considerations. NICEATM is currently co-organizing an international workshop on human and veterinary vaccine testing focusing on rabies vaccines. HSUS encourages and would be happy to help with further work in the area of vaccines by NICEATM and ICCVAM members.

Encourage the establishment of grant review criteria tailored to the development of alternative methods.

As ICCVAM's roadmap points out, one way to facilitate funding of NAMs is to modify grant review criteria. As ICCVAM is housed within an NIH institute, it could also encourage the issuance of specific grant opportunities for development of NAMs. NICEATM might also play a larger role in influencing approaches taken by NTP more generally, which could, when successful, influence the investment in NAMs by other institutes. ICCVAM should explore additional approaches for funding NAMs.

¹ Guidance for Waiving Acute Dermal Toxicity Tests for Pesticide Formulations and Supporting Retrospective Analysis. 2016. Available: <https://www.epa.gov/pesticide-registration/bridging-or-waiving-data-requirements>

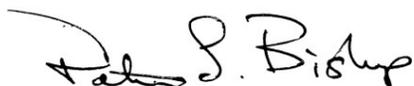
Strategic goal: Encourage the adoption and use of new methods and approaches by federal agencies and regulated industries

Collaborate with international partners to facilitate global harmonization and regulatory acceptance.

As global acceptance and harmonization of testing methods and requirements will play an essential role in the widespread uptake of NAMs, we strongly encourage ICCVAM and its federal member agencies to increase involvement with OECD and the International Cooperation on Alternative Test Methods (ICATM), whenever possible. OPP has often taken the lead; however, NAMs implementation would benefit from the committed participation of other ICCVAM members.

We are eager to help ICCVAM in further dissemination and uptake of these approaches in the United States and globally, whether in the form of webinars, agency trainings, outreach to international partners, or in organizing further workshops.

Sincerely,



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